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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/078,927	02/19/2002	Thomas Curran	SJ-01-0032	6357

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 01/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/078,927	CURRAN ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,23,25 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,23,25 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 1-15, 23, 25, and 32 are pending in the application.

[2] The amendment to the claims, filed December 13, 2004, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[3] The amendment to the specification, filed December 13, 2004, is acknowledged.

[4] Applicant's arguments filed December 13, 2004 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Rejections - 35 USC § 112, Second Paragraph

[6] The rejection of claims 1 (claims 3-6, 11, and 13-14 dependent therefrom), 2, 7-10, 12, 15, 23, 25, and 31 as being indefinite in the recitation of "Cdk5," "Cdk5 activity," and "Dab1" is maintained for the reasons of record and the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue terms "Cdk5" and "Dab1" are allegedly familiar, well-known terms. Addressing "Cdk5," applicants argue "Cdk5" is distinguished from other Cdk's by virtue of its not being involved in cell cycle regulation, its active form being found only in differentiated neurons of the developing and mature brain, and that Cdk5 is activated by p35. Addressing "Dab1, applicants argue the

homology between Dab1 and Dab2 "break[s] down after the first 170 amino acids," particularly the region of Dab1 that is phosphorylated by Cdk5. Applicants assert the invention is not based on the discovery of Dab1 or Cdk5 proteins or activities, but on the alleged discovery that Dab1 is phosphorylated by Cdk5.

Applicants' argument is not found persuasive. The examiner acknowledges applicants' admission that Dab1 and Cdk5 were known in the art at the time of the invention and further acknowledges the claims are drawn to methods for detecting Cdk5 activity by detecting Dab1 phosphorylation. However, even in view of applicants' alleged distinguishing characteristics of Cdk5 and Dab1, it remains unclear as to the scope of proteins that are intended as being encompassed by the terms "Cdk5" and "Dab1" and what activity or activities is/are encompassed by the term "Cdk5 activity." Applicants assert the specification and prior art teach many properties of a protein that is considered to be a "Cdk5" or "Dab1" protein (see above), however, the specification fails to define which of these are necessary for inclusion of a cyclin-dependent kinase or a disabled-1 protein which is distinct in sequence from similar proteins that may share these characteristics. For example, is the intended scope of Cdk5 proteins any protein that phosphorylates Dab1, is not involved in cell cycle regulation, is active only in differentiated neurons of the developing and mature brain, and is activated by p35? In this case, the claims are not so limited and it is noted that these characteristics are not included in the definition provided for "Cdk5" in the specification, *i.e.*, "a protein with serine/threonine kinase activity that is structurally homologous to the mitotic cyclin dependent kinase." It is noted that there is no indication as to how "structurally

homologous" a sequence must be or an indication as to a reference sequence that is useful in determining such structural homology. Also, is the intended scope of Dab1 proteins any protein that is phosphorylated by Cdk5 and whose structural homology "break[s] down after the first 170 amino acids," particularly the region of Dab1 that is phosphorylated by Cdk5? Again it is noted that the claims are not so limited and it is noted that these characteristics are not included in the definition provided for "Dab1" in the specification, *i.e.,* "an intracellular adapter protein that is phosphorylated by Cdk5 activity and by reelin tyrosine kinase activity." It is noted that there is no definition provided in the specification for those proteins that have "Cdk5 activity" or "reelin tyrosine kinase activity." Further, as stated in a previous Office action, it is unclear as to whether the terms are meant to encompass those Cdk5's or Dab1's that are considered to be "naturally-occurring" or to also encompass those that are mutants and/or fragments of a known Cdk5 or Dab1 protein. It is suggested that applicants clarify the scope of polypeptides that are considered to be a "Cdk5" or "Dab1" polypeptide by, for example, identifying their intended Cdk5 or Dab1 polypeptide by a sequence identifier.

[7] The rejection of claims 1 (claims 2, 4-9, 11-15, 23, and 25 dependent therefrom), 10 (claims 12-15 dependent therefrom), and 31 as being indefinite in the recitation of "a candidate sequence preferred by cdk5 activity" is maintained for the reasons of record and the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue claims 1, 9-10, and 12 "have been amended to show that a serine within a candidate sequence is the site of Cdk5 phosphorylation," the specification defines "candidate sequence" as containing a serine

followed by proline at the +1 position and a lysine in the +3 position, and that applicants predicted that serines 481 and 515 of murine Dab1 to be Cdk5 phosphorylation sites.

Applicants' argument is not found persuasive. The examiner acknowledges the amendment to claims 1, 9-10, and 12 and further acknowledges the definition of the term "candidate sequence" at page 5 of the specification. However, this definition provides no indication as to the scope of those candidate sequences that are "preferred" by a "cdk5 activity." Thus, even in view of the amendment, the claims remain indefinite in the recitation of "a candidate sequence preferred by cdk5 activity," particularly in view of the indefiniteness of the term "cdk5 activity" as described above and in a previous Office action and that the scope of candidate sequences are those that are "preferred" by cdk5 activity. It is unclear from the specification and the claims as to whether all sequences that have a serine followed by proline at the +1 position and a lysine in the +3 position are those that are "preferred" by a "Cdk5 activity" or whether only a subset of those sequences that have a serine followed by proline at the +1 position and a lysine in the +3 position are meant to be encompassed as being sequences that are "preferred" by "cdk activity." It is suggested that applicants clarify the meaning of the term.

[8] The rejection of claims 4-6 as being are unclear in the recitation of "derived from" is maintained for the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue a dictionary definition of the term is "to get or obtain something from something else" and the term is well-known as meaning "tissues, blood, etc. isolated directly from a subject as well as other

substances...which are derived from the directly isolated tissues." Applicants argue the examiner's stated interpretation of the term as meaning "isolated from" does not adequately reflect the scope of samples to which the claimed method can be applied. Applicants further argue the term allegedly appears in "over 3000 patents issued in the year 2004."

Applicants' argument is not found persuasive. Addressing the use of the term in issued patents, it is noted that each patent application is examined on its own merits. For example, the term may be specifically defined or may have been clarified during prosecution to have a definite meaning in patent applications that issued as patents. However, the meaning of the term "derived from" is not clarified in the specification, or by applicants' explanation. In the instant case, the examiner's interpretation of the term, *i.e.,* "isolated from," does not contradict with applicants' intended meanings of "to get or obtain something from something else" and "tissues, blood, etc. isolated directly from a subject as well as other substances...which are derived from the directly isolated tissues." However, in view of applicants' assertion that "isolated from" does not reflect the scope of samples to which the method can be applied, it remains unclear as to the scope of the term "derived from," particularly as applicants make no mention of or attempt to distinguish those samples that are "derived from" the recited organism that are not considered to be "isolated from" the recited organism. Applicants are requested to clarify the scope of "samples to which the claimed method can be applied" that are "derived from" the recited organism.

[9] The following new rejection under 35 USC 112, second paragraph, is necessitated by amendment. Claims 2, 12, and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] Claim 2 is indefinite in the recitation of "murine Dab1" as the specification fails to disclose those characteristics that distinguish a "murine" Dab1 protein from other Dab1 proteins. It is suggested that applicants clarify the scope of intended Dab1 polypeptides by, for example, identifying a "murine Dab1" by a sequence identifier.

[b] Claim 2 is indefinite in the recitation of "the candidate sequence is included within the Dab1 amino acids selected from..." The meaning of the term is unclear. In order to clarify the meaning of the term, it is suggested that applicants amend the term to recite, for example, "the candidate sequence selected from the group consisting of...is included within the amino acid sequence of Dab1" or "the candidate sequence is included within the amino acid sequence of Dab1, wherein the candidate sequence is selected from the group consisting of..."

[c] Claim 12 is unclear in the recitation of "serine contained within the amino acids...of SEQ ID NO:1 and SEQ ID NO:2" as it is unclear as to the serine of SEQ ID NO:1 or 2 to which applicants refer as being phosphorylated in the sequence of SEQ ID NO:1 or 2 as SEQ ID NO:1 and 2 each comprises at least three different serine residues. It is suggested that applicants clarify the intended serine of SEQ ID NO:1 and 2.

[d] Claim 32 is indefinite in the recitation of "GenBank accession number 1771281" as it is unclear as to the scope of sequences that are referenced by GenBank accession number 1771281. It is well-known to one of skill in the art that sequence accession numbers are updated by modifying the sequence of a particular accession number. For example, based on the latest revision history for GenBank accession number 1771281, it appears this accession number has been modified no less than 4 times. Furthermore, it is noted that "GenBank accession number 1771281" lists the sequence of a polypeptide referred to as "mDab555," not Dab1. As such, it is unclear as to the scope of polypeptides that are encompassed by the term "GenBank accession number 1771281." It is suggested that, for example, applicants identify the sequence of mouse Dab1 having GenBank accession number 1771281 by a sequence identifier.

Claim Rejections - 35 USC § 101

[10] The rejection of claims 23 and 25 under 35 U.S.C. 101 and the corresponding enablement rejection of claims 23 and 25 under 35 U.S.C. 112, first paragraph, are maintained for the reasons of record and the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue deregulation of Cdk5 activity is allegedly associated with Alzheimer's disease and that lack of Cdk5 activity in mice is allegedly associated with several neurodegenerative diseases, citing Patrick et al. *Nature* 402:615-622 and Ohshima et al. *PNAS* 93:11173-11178 (both cited in the IDS filed March 25, 2002). Applicants argue that an assay for quantitatively measuring Cdk5 activity "provides a very useful tool for detecting neurological disorders" and that

"compounds that inhibit Cdk5 activity may prove useful therapeutics to treat this disease."

Applicants' argument is not found persuasive. As an initial matter, it is noted that the rejections of original claims 1-15 and 31 have been withdrawn. Claims 1-15 and newly added claim 32 are drawn to methods for detecting Cdk5 activity. A detailed review of the reference of Patrick et al. indicates the reference teaches that patients with Alzheimer's disease have been shown to have an increased accumulation of p25, a truncated form of p35, which activates Cdk5. Patrick et al. disclose the deregulation of Cdk5 activity due to the presence of p25 results in damage to the cytoskeleton and neuronal death, which are fundamental characteristics of some neurodegenerative diseases. Thus, at least based on the evidence of Patrick et al., deregulation of Cdk5 kinase activity appears to be correlated with the presence of Alzheimer's disease. As such, one could use the claimed methods for screening for agents that decrease Cdk5 activity.

However, it is noted that neither the specification nor the prior art provide sufficient guidance for using the methods of claims 23 and 25 for detecting neurological disorders. For example, what is the threshold level of increased Cdk5 activity that would indicate the presence of a neurological disorder and which neurological disorder(s)? In other words, what level of increased Cdk5 activity as compared to a control would be indicative of a neurological disorder? Is any increase in Cdk5 activity indicative of a neurological disorder or is a significant increase required? As sufficient guidance has not been provided in the specification and/or prior art, it is the examiner's position that

further experimentation is required to identify a "real world" use for the claimed invention. See Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). The specification must teach a skilled artisan how to use what is claimed. As such, the asserted utility for claims 23 and 25 is not substantial.

Claim Rejections - 35 USC § 112, First Paragraph

[11] The written description rejection of claims 1-15, 23, 25, and 32 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue the invention is not based on the novelty of Cdk5 or Dab1, but rather on their relationship. Applicants argue the terms "Cdk5" and "Dab1" have "distinct meanings well known by those skilled in the art" and "[m]embers of each respective family have common structure, characteristics and activities which form the basis of their classification."

Applicants' argument is not found persuasive. The examiner acknowledges the invention is not drawn to Cdk5 or Dab1, but to methods for detecting Cdk5 activity based on Dab1 phosphorylation. However, while the claims are not drawn to Cdk5 or Dab1 polypeptides, it is the examiner's position that these are an essential and critical feature of the claimed methods and therefore, according to MPEP 2163, must be adequately described. Contrary to applicants' assertion there is no disclosure in the specification of a structure-function correlation between the members of the respective genus of Cdk5 or Dab1 polypeptides such that by the mere recitation of "Cdk5" or

"Dab1" one of skill can visualize the structures of all members of the respective genus, particularly in view of the indefiniteness of the terms "Cdk5" and "Dab1" as stated above. It is noted that, while applicants assert "[m]embers of each respective family have common structure, characteristics and activities," applicants fail to point out the disclosure of such common structural characteristics in the specification, *i.e.,* what common structural characteristics are shared by all members of the respective genus? Even assuming *arguendo* the specification disclosed structural characteristics that are shared by all members of the respective genus, the claims are not so limited to Cdk5 or Dab1 polypeptides having common structural characteristics.

Applicants argue that in view of the alleged shared structural and functional features of Cdk5 and Dab1 proteins, one of skill would expect Cdk5 phosphorylation of Dab1 to be shared by other members of this family. Applicants argue the examiner has set forth no rationale as to why such an event would not occur with other Cdk5-Dab1 species combinations.

Applicants' argument is not found persuasive. The examiner has not questioned the operability of the invention in the instant rejection. It appears applicants' argument is directed to the utility and/or scope of enablement rejection and not the instant written description rejection. In this case, the rejection is based upon the failure of the disclosed representative species, *i.e.,* the three disclosed representative species of Cdk5 polypeptides, *i.e.,* human Cdk5 having GenBank accession number 4826674, mouse Cdk5 having GenBank accession number 6680907, and rat Cdk5 having GenBank accession number 203389 and the two disclosed representative species of Dab1

polypeptides, *i.e.,* human Dab1 having GenBank accession number 3288851 and mouse Dab1 having GenBank accession number 1771281, to describe all members of the respective genus, which encompasses species that are widely variant, particularly in view of the indefiniteness of the terms "Cdk5" and "Dab1."

Applicants argue it is not necessary to disclose each and every species of a genus. Applicants argue structural, physical, and chemical properties of Cdk5 and Dab1 polypeptides are allegedly well known and methods are known for identifying all members of the genus, "whether they be novel or mutants and variants of known Cdk5 or Dab1 polypeptides" that possess these properties.

Applicants' argument is not found persuasive. The examiner acknowledges that disclosure of all species encompassed by a recited genus is not necessary as only a representative number of species sufficient to describe all members of a genus is required for adequate written description. However, as stated above, the disclosed representative species of Cdk5 and Dab1 polypeptides fails to represent all members of the recited genus, which, as acknowledged by applicants, encompasses widely variant species including those polypeptides that are considered to be Cdk5 and Dab1 polypeptides that are yet to be isolated and mutants and variants of known and yet to be isolated Cdk5 and Dab1 polypeptides. Contrary to applicants' assertion, there is no disclosed structure-function correlation among Cdk5 or Dab1 polypeptides in the specification or prior art. As such, applicants have failed to adequately describe the recited genus of Cdk5 or Dab1 polypeptides, which encompasses widely variant species.

Regarding the genus of recited antibodies, applicants argue one of skill in the art is capable of determining if a Dab1 protein contains a "preferred" Cdk5 candidate sequence and generating antibodies to this sequence and it is not necessary that all species encompassed by the genus be disclosed.

Applicants' argument is not found persuasive. It is noted that the genus of recited antibodies is not limited to those that bind to a "candidate sequence" of Cdk5, but is a genus of antibodies that binds to a phosphorylated or unphosphorylated Dab1 polypeptide. In this case, the genus of recited antibodies that binds to a "Dab1" protein is widely variant, particularly in view of the indefiniteness of the scope of polypeptides that are considered to be "Dab1" polypeptides as stated above. As such, the single disclosed representative species of the genus of recited antibodies, *i.e.,* a phosphoserine antibody generated against SEQ ID NO:3 with a phosphorylated serine at position 8, fails to adequately describe all members encompassed by the genus of recited antibodies.

[12] Even if applicant demonstrates the methods of claims 23 and 25 have a specific and substantial or well-established utility, the following rejection is maintained. The scope of enablement rejection of claims 1-15, 23, 25, and 32 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below.

RESPONSE TO ARGUMENT: Regarding the amount of guidance and working examples, applicants argue Cdk5 and Dab1 are well known, a preferred candidate sequence is well known, methods for identifying a preferred candidate sequence within a protein are well known, and methods for detecting phosphorylation of a protein at a

specific site and generation of reagents to do so are familiar techniques to one of skill in the art. Applicants request the examiner to provide evidence why a skilled artisan would not expect any Cdk5 to phosphorylate Dab1 on a serine within the candidate sequence taught and why methods for detecting phosphorylation would not be expected. Regarding claims 23 and 25, applicants argue the Cdk5 activity has been associated with Alzheimer's disease and amyotrophic lateral sclerosis. Applicants' argument is not found persuasive.

As an initial matter, it is noted that it is unclear to the examiner as to the scope of proteins that are considered to be "Cdk5" or "Dab1" polypeptides and it is unclear as to those "preferred" candidate sequences, particularly in view of the indefiniteness of the terms. Contrary to applicants' assertion, the scope of proteins considered to be Cdk5 and Dab1 are not well known, and those candidate sequences that are considered to be "preferred" by "cdk activity" are not well known. As stated in a previous Office action, the specification is enabling only for a method for detecting the presence of Cdk5 kinase activity by immunoprecipitating human Dab1 having GenBank accession number 3288851 or mouse Dab1 having GenBank accession number 1771281 from a biological sample with or without Cdk5; contacting the immunoprecipitated Dab1 with a phosphoantibody, generated using SEQ ID NO:3 with a phosphorylated serine at position 8 as an antigen; detecting binding of the phosphoantibody to serine 491 and/or 515 of Dab1, wherein increased binding of the phosphoantibody to serine 491 and/or 515 of Dab1 in a biological sample with Cdk5 as compared to a sample without Cdk5 indicates the presence of Cdk5 kinase activity in said sample, does not reasonably

provide enablement for the broad scope of claimed methods. To the extent the examiner understands applicants' request, it is noted that the alleged novel relationship that applicants refer to, *i.e.,* the phosphorylation of Dab1 by Cdk5, has not been shown in all organisms that express "Cdk5" and "Dab1" polypeptides. Even assuming *arguendo* Cdk5 phosphorylated the corresponding Dab1 within all organisms, due to structural differences that are likely to occur among the different organisms, it is unclear as to whether any Cdk5 from any organism will phosphorylate any Dab1 from any other species. Furthermore, it is noted that; as acknowledged by applicants, the claims encompasses mutant and variant Cdk5 and Dab1 polypeptides. There is no indication that the method will be so useful in measuring activity of mutant and variant Cdk5's or that the method using a mutant Dab1 polypeptide will be so useful for measuring a "wild-type" or mutant Cdk5. Applicants request for evidence is acknowledged. The examiner can provide no evidence to support such unpredictability. However, one of skill in the art would recognize such unpredictability, particularly as the method is dependent upon a biological relationship. It should be noted that applicants have failed to support their position that any Cdk5, having any sequence from any source, can phosphorylated any Dab1, having any sequence from any source. Applicants are reminded that arguments of counsel alone cannot take the place of evidence. Regarding claims 23 and 25, again it is noted that no working example for "detecting a neurological disorder" has been disclosed. Applicants are invited to direct the examiner's attention to such a working example.

Addressing the high level of unpredictability in the art, applicants again argue Cdk5 and Dab1 are well known, a preferred candidate sequence is well known, methods for identifying a preferred candidate sequence within a protein are well known, and methods for detecting phosphorylation of a protein at a specific site and generation of reagents to do so are familiar techniques to one of skill in the art. Regarding claims 23 and 25, applicants argue Patrick et al. (supra) allegedly shows a correlation between increased Cdk5 activity and Alzheimer's disease, Nguyen et al. allegedly shows that unregulated Cdk5 activity is implicated in amyotrophic lateral sclerosis, and additional references of Appendix A allegedly show that Cdk5 is related to ischemic injury, neurofibrillary pathology, and Niemann-Pick type C disease.

Applicants' argument is not found persuasive. As stated above, it is noted that it is unclear to the examiner as to the scope of proteins that are considered to be "Cdk5" or "Dab1" polypeptides and it is unclear as to those "preferred" candidate sequences, particularly in view of the indefiniteness of the terms. Contrary to applicants' assertion, the scope of proteins considered to be Cdk5 and Dab1 are not well known, and the scope of "preferred" candidate sequences is not well known. While Cdk5 and Dab1 proteins and a single preferred sequence may have been known in the art or disclosed in the specification at the time of the invention, the claims are not so limited. In this case, it is highly unpredictable as to whether a "Cdk5" from any source, including mutants and variants thereof, will phosphorylate a "Dab1" from any source, including mutants and variants thereof. Also, it is highly unpredictable as to whether phosphorylated Dab1 from any source is related only to Cdk5 phosphorylation as it is

likely that Dab1 is phosphorylated by other kinases in other organisms. Regarding claims 23 and 25, it is noted that it is highly unpredictable as to whether increased Cdk5 activity is associated with *any* neurodegenerative disorder. The cited references fail to rebut this assertion. Further, it is noted that some of the cited references were made publicly available *after* the filing date of the instant application and the specification should enable the full scope of the claimed invention at the time of filing. Even assuming increased Cdk5 activity was associated with *any* neurodegenerative disorder, it is noted that the specification fails to provide even a single working example and/or guidance for detecting even a *single* neurodegenerative disorder. Applicants are invited to direct the examiner's attention to such a working example.

Addressing the amount of experimentation, applicants argue the amount of experimentation required to practice the full scope of claims 23 and 25 is routine as Cdk5 activity is allegedly associated with multiple neurological disorders. Applicants argue that "[k]nowing whether a sample has increased Cdk5 activity provides useful information which can be taken into account when diagnosing a subject or considering treatment options."

Applicants' argument is not found persuasive. It is noted that applicants do not dispute the examiner's assertion that "[i]t is not routine in the art to screen proteins from all sources to determine whether such proteins will be specifically phosphorylated by a kinase and to determine all methods of detecting specific phosphorylation thereof." Addressing claims 23 and 25, it is noted that, while Cdk5 *may* be associated with multiple neurological conditions, this is no indication that it is associated with *all*

neurological conditions. As stated above, the specification fails to provide even a single working example for practicing the claimed method. Applicants are invited to direct the examiner's attention to such a working example in the specification. Thus, it is not even clear that increased levels of Cdk5 activity can be used to detect a neurological disorder, and even if they can, the specification fails to provide the necessary guidance for determining whether one has a neurological disorder based on increased levels, *e.g.*, what level of increased Cdk5 activity as compared to a control is indicative of a neurological disorder, and if one has a neurological disorder, which disorder?

At least for the reasons of record and the reasons stated above, undue experimentation would be required for a skilled artisan to make and/or use the full scope of the claimed methods.

Conclusion

[13] Status of the claims:

Claims 1-15, 23, 25, and 32 are pending.

Claims 1-15, 23, 25, and 32 are rejected.

No claim is in condition for allowance.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Thursday and on alternate Fridays from 7:30 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

01-20-05

DAVID J. STEADMAN, PH.D.
PRIMARY EXAMINER